

PCT

世界知的所有権機関

国際事務局

特許協力条約に基づいて公開された国際出願



(51) 国際特許分類6 C12N 15/11, C12Q 1/68 // G01N 33/566	A1	(11) 国際公開番号 WO 95/14772 (43) 国際公開日 1995年6月1日 (01.06.95)
(21) 国際出願番号 PCT/JP94/01916 (22) 国際出願日 1994年11月11日(11.11.94) (30) 優先権データ 特願平5/355504 1993年11月12日(12.11.93) JP (71) 出願人：および (72) 発明者 松原謙一(MATSUBARA, Kenichi)[JP/J] 〒565 大阪府吹田市山田東3-18-1-804 Osaka, (JP) 大久保公策(OKUBO, Kousaku)[JP/J] 〒562 大阪府箕面市瀬川2-11-26 Osaka, (JP) (74) 代理人 弁理士 吉田研二, 外(YOSHIDA, Kenji et al.) 〒180 東京都武蔵野市吉祥寺本町1丁目34番12号 Tokyo, (JP)	(81) 指定国 AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN, 欧州特許(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許(BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO特許(KE, MW, SD, SZ). 添付公開書類 国際調査報告書 補正書	
(54) Title : GENE SIGNATURE (54) 発明の名称 ジーン・シグナチャー (57) Abstract A 3'-directed cDNA library which accurately reflects the abundance ratio of mRNA in a cell has been prepared from various human tissues, and sequencing of the cDNAs contained in the library has been conducted to examine the incidence of each cDNA in each tissue. As each cDNA has expression information with each tissue corresponding to the mRNA concentration, these cDNAs are usable as a probe or primer for detecting cell anomaly or discriminating cells. The cloned gene can produce proteins utilizable as a medicine or the like.		

TAATCANTGT TATTGTGTTC CANTTTAACT GGGTTAAATG TTN

284

配列番号 : 3190

配列の長さ : 282

配列の型 : 核酸

トポロジー : 直鎖状

クローン名 : HUMGS03761

配列 :

```
GATCTCGACT CCCCCCTGGC CACAGACCCC CAGGTCATTG TGTTCACTGT ACTCTGTGGG 60
CAAGGATGGG TCCAGAAGAC CCCACTTCAG GCACTAAGAG GGGCTGGACC TNTGCGGCAG 120
GAAGCCAAAG AGACTGGGCC TAGGCCAGGA GTTCCCAAAT NTGAGGGGCG AGAAACAAGA 180
CAAGCTCCTC CCTTGAGAAT TCCCTGTGGA TTTTAAAAC AGATATTATT TTTNTNATTA 240
TTGTGACAAA ATGTTGNTAA ATGGGATATT AAATAGAATA AA 282
```

配列番号 : 3191

配列の長さ : 279

配列の型 : 核酸

トポロジー : 直鎖状

クローン名 : HUMGS03762

配列 :

```
GATCTGGAGA AGTAAGATGG CCAAATAAAA GCCTCTACCA ATCATCCTCC CCACAGGAAC 60
ACCAAATTTA AGAACTATCT ACACAAAAAA GCACCTTCAT AAGAACCAAA AATCAGAGAG 120
AACAAGGATA AAGAAGTATC CAAATACAAA GAAAATGTTA TGCAAGTGAC CTTTAGAGAT 180
GTTTTAAAGA TGACAAAATA TTGATGANGA TGGGCCAACA AGTGTTACTG TTACCTCTAA 240
TAAAGTTTCA TCACTAGTTT CACCATGGTT AATTGAAA 279
```

配列番号 : 3192

配列の長さ : 277

配列の型 : 核酸

トポロジー : 直鎖状

クローン名 : HUMGS03763

配列 :

```
GATCTGCTCA AATGCACCAA CACTGCCAAG TGACTAAGGT AGAAAAGAAA AATAACAGGT 60
ATCGTCATCT GAAGGACAGA TGAATCTTTT TCTGCCCCCT CTTCACAATG GAATATAAGG 120
AACAATTATG GGATGTCATC AGAATGGATG CCATAGGACC TACAGCTCCC TTTCTNTTTA 180
TTGTNATTAT ACTTTAAATA TGACATTGTC TTTNATGTGT ATGTTCTAT ATTTCAATG 240
TATCTTTTTT CTTCAGTAAA CCTGATATTC AAATAAA 277
```

配列番号 : 3193

配列の長さ : 277

配列の型 : 核酸

トポロジー : 直鎖状

クローン名 : HUMGS03764

配列 :

```
GATCACAGGG AGCCTGTGTT TGTTGGAGGT GTTCCAGAAT CTNACTGAC ACCACGCTTG 60
```

450	CAGGACGGAGCGCAGGAGTGTGGACGGGACAGTGCAGTGGCTGGGAGGAGCCAGAATC	51
241	CAGGATGGAGCACAAGCAGGTGTGGATGGACAGTCAGTGGCTGGAGAGACCAAAATC	30
520	AACAGCTCCAGCCCTCTGGCTACACCCGCCAGATCGGGAGCTTTATAGTCACCCGGGCT	57
301	AACAGCTCCAGCCCTCTGGCTACGACGCCAGATGGGGAAATTTACAGTCATCAGGCT	36
580	GGGCTCTACTACCTGTACTGTCTCAGGTGCACCTTTGATGAGGGGAAGGCTGTCTACTCTGAAG	63
361	GGGCTCTACTACCTGTACTGTCTCAGGTGCACCTTTGATGAGGNAAGGCTGTCTACTCTGAAG	42
640	CTGGACTTTCGTGGTGGATGGTGTCTGGCCCTGCCCTGCCCTGGAGGAATTCACGCCACT	69
421	CTGGACTTTCGTGGTGAACGGTGTCTGGCCCTGCCCTGCCCTGGAGGAATTCACGCCACA	48
700	CGCGCCAGTTTCCCTCGGGGCCCCAGCTCGCCCTCTGCCAGGTGTCTGGGCTGTGGCCCTG	75
481	GCAGCAAGCTCTCCCTGGGCCCCAGCTCGTGTGCGCAGGTGTCTGGGCTGTGGGCGCTG	54
760	CGGCGCAGGTCTCCCTCGGGATCGCACCCCTCCCTGGGCCCATCTCAAGGCTGCCCCC	81
541	CGGCCAGGGTCTTCGCTTCGGATCGCACCCCTCCCTGGGCTCATCTTAAGGCTGCCCC	60
820	TTCCCTCACCCTACTTCGGACTCTTCAGGCTTCACGTGAGGGGCCCTGTGCTCC	871
601	TTCCPAACCTACTTTGGACTCTTTCAGGCTTCACGTGAGGGGCCCTGTGCTCTCC	652
RESULT	6	
T22190	T22190 standard; cDNA to mRNA; 282 BP.	
T22190	C	
T27-AUG-1996	(first entry)	
Human gene signature	HUMGS03761.	
Gene signature	mRNA; relative abundance; frequency;	
human; cloning; mapping; non-biased library;	diagnosis; detection;	
cell typing; abnormal cell function; ss.		
W09514772-A1.		
01-JUN-1995.		
11-NOV-1994.		

```

PR 12-NOV-1993; JP-355504.
PA (MATSU) MATSUBARA K.
PA (OKUBU) OKUBO K.
PI Matsubara K, Okubo K;
DR WPI; 95-206931/27.
PT Identifying gene signatures in 3'-directed human CDNA library - e.g.
PT for diagnosis of abnormal cell function, by preparing cDNA that
PT reflects relative abundance of corresp. mRNA in specific human
PT tissues
PS Claim 1; Page 1067; 2245pp; Japanese.
CC A single-stranded DNA (or its complementary strand or the corresp.
CC double-stranded DNA) which comprises one of the 7837 "GS" sequences
CC given in T19001-T26837 and which is able to hybridize to part of
CC human genomic DNA, cDNA or mRNA is claimed. The GS (Gene Signature)
CC sequences were obtained from 3'-directed cDNA libraries prepared
CC from various human tissues; synthesis of cDNA was initiated from the
CC 3'-end of mRNA by using poly(T) as the sole primer. Since the 3'-
CC untranslated sequence is unique to a particular mRNA species, almost
CC all the 3'-oriented cDNAs hybridize with specific mRNAs. Each library
CC is constructed so as to reflect accurately the relative abundance of
CC different mRNAs in the particular tissue from which it was derived.
CC The appearance frequency of a given GS in a cDNA library can be
CC determined (esp. using primers and probes derived from the GS
CC sequences) as a means of diagnosing abnormal cell function or for
CC recognising different cell types.
SQ Sequence 282 Bp; 80 A; 62 C; 69 G; 66 T;

Query Match 17.9%; Score 245.4; DB 1; Length 282;
Best Local Similarity 97.3%; Pred. No. 1e-42;
Matches 257; Conservative 0; Mismatches 6; Indels 1; Gaps 1;

QY 1111 GATCTGACTCCCTCCCTGGCCACAGACCCCGGCGGCTGTTCACTGTTCTGTGGG 1170
DB 1 GATCTGACTCCCTCCCTGGCCACAGACCCCGGCGGCTGTTCACTGTTCTGTGGG 60

QY 1171 CAAGGATGGTCCAGAGACCCCTTCCAGGCTTCCAGGAGGCTGACCTG-GCGGCAG 1229
DB 61 CAAGGATGGTCCAGAGACCCCTTCCAGGCTTCCAGGAGGCTGACCTGTTGGCGAG 120

QY 1230 GAAGCCAAAGAGACTGGGCTTGGCCAGGAGTTTCCAAATGTGAGGGCGGAGAACAGA 1289
DB 121 GAAGCCAAAGAGACTGGGCTTGGCCAGGAGTTTCCAAATGTGAGGGCGGAGAACAGA 180

QY 1290 CAAGCTCTCTCCCTGAGAAATTCCTGTGGATTTTAAACAGATATATTTTATTATTA 1349
DB 181 CAAGCTCTCTCCCTGAGAAATTCCTGTGGATTTTAAACAGATATATTTTATTATTA 240

QY 1350 TTGTGACAAAATGTTGATAATGG 1373
DB 241 TTGTGACAAAATGTTGATAATGG 264

RESULT 7
X53491/c
ID X53491 standard; DNA; 114955 Bp.
AC X53491.
DE 05-JUL-1999 (first entry)
DE Human adenosine A1 receptor antisense oligonucleotide fragment.
KW Antisense oligonucleotide; multiple target; antisense treatment;
KW impaired respiration; inflammation; lung disease;
KW pulmonary vasoconstriction; inflammation; allergic rhinitis;
KW acute asthma; allergy; asthma; impeded respiration;
KW respiratory distress syndrome; pain; cystic fibrosis;
KW pulmonary hypertension; pulmonary vasoconstriction; emphysema;
KW chronic obstructive pulmonary disease; leukemia; lymphoma; carcinoma;
KW colon cancer; breast cancer; lung cancer; pancreatic cancer;
KW hepatocellular carcinoma; kidney cancer; melanoma; hepatic metastasis;
KW prostate cancer; ss.
OS Synthetic.
RN W09913886-Al.
EN 25-MAR-1999.
PR 17-SEP-1997; US-059160.
PA (UYEC-) UNIV EAST CAROLINA.
PI Nyce JW.
DR WPI; 99-229400/19.
PT New antisense oligonucleotides used in treatment of, e.g. pulmonary
PT vasoconstriction
PS Disclosure; Page 37; 120pp; English.
CC The specification describes antisense oligonucleotides (X52869-X55271)
CC directed against at least 2 mRNAs selected from target genes, coding and
CC non-coding regions of RNAs corresponding to target genes, gene
CC initiation codons, genomic flanking regions, intron-exon borders, the
CC 5'-end, the 3'-end and the junction between coding and non-coding
CC regions and all segments of RNAs encoding proteins associated with one
CC or more diseases, conditions or mixtures. The antisense oligonucleotides
CC may be derived from sequences X55272-74. These multiple target
CC oligonucleotides (specifically X55180-271) can be used for the antisense
CC treatment of diseases and conditions. Typical diseases and conditions
CC are those associated with impaired respiration and inflammation,
CC including lung diseases, pulmonary vasoconstriction, inflammation,
CC allergic rhinitis, acute asthma, allergies, asthma, impeded respiration,
CC respiratory distress syndrome, pain, cystic fibrosis, pulmonary
CC hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive
CC pulmonary disease (COPD), and cancers such as leukemias, lymphomas,
CC carcinomas e.g. colon cancer, breast cancer, lung cancer, pancreatic
CC cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic
CC metastases, as well as all types of cancers which may metastasize or have
CC metastasized to the lungs, including breast and prostate cancer.
SQ Sequence 114955 Bp; 6071 A; 29417 C; 36712 G; 21328 T;

Query Match 5.1%; Score 70.4; DB 1; Length 114955;
Best Local Similarity 32.7%; Pred. No. 6.5e-06;
Matches 182; Conservative 58; Mismatches 316; Indels 0; Gaps 0;

QY 26 CCGCCCGCCGCGCTCCCTCCCGGATCCCTCGGGTCCCGGGATGGGGGCGGTGAGGC 85
DB 105272 CCGCCCGCGCGCGCNHNNHNSCGCGCGCGCGCGCGCNHNNHNSCGCGCGCGC 105213

QY 86 AGGCACAGACCCCGCCCATGCGCCCGCTGCGGACCGAGCGGCGGCGCGCGG 145
DB 105212 CCGCGCGCGCGCNHNNHNSCGCGCGCGCGCGCGCGCNHNNHNSCGCGCGCGC 105153

QY 146 GGGAGCGCGCGCGCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 205
DB 105152 GCGCGCGCGCGCGCNHNNHNSCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGC 105093

QY 206 GCCTCGCGCTCTCTGCTGCGCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 265
DB 105092 GCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 105033

QY 266 AGCTGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 325
DB 105032 CCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 104973

QY 326 AGACAGAGAAAGACGAGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 385
DB 104972 CCVGNHNNHNSCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 104913

QY 386 GTGCACCTAAAGCGCGGAAACACGGGCTCGAAGAGCGATCGAGCCCATTTATGAAGTTC 445
DB 104912 CCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 104853

QY 446 ATCCACGACCTGGACAGGACCGAGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 505
DB 104852 VGGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 104793

QY 506 AGGAAGCCAGAAATCAACAGCTCCAGCCCTCTGCGCTACACCGCAGATCGGGAGTTTA 565
DB 104792 VGGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCG 104733

QY 566 TAGTCACCGCGCGCTGG 581

```